

**REMARKS**Elections/Restrictions

The Examiner has stated that claims 24, 30, 36, and 38-48 are drawn to an invention nonelected with traverse in Paper No. 8. (8/26/03 OA, page 2, second paragraph.) Claims 24, 30, 36, and 38-48 have been canceled without prejudice.

Claim Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 10, 17, 25, 31, and 37 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regards as the invention. Claims 10, 17, 25, 31, and 37 have been canceled without prejudice.

Claim Rejections Under 35 U.S.C. § 103(a)

Claims 1-23, 25-29, 31-35 and 37 remain rejected under 35 U.S.C. § 103(a), as allegedly unpatentable over JP 57167938, GB1476016, or JP 352102434 taken with JP 11236334 or JP 52145509. Applicants respectfully traverse this rejection.

According to the abstract provided with the 3/5/03 office action, JP 57-167938 discloses two new diterpenoids allegedly having carcinostatic activity. The abstract states that oridonin is known to exhibit carcinostatic activity. A procedure for isolating the novel compounds is provided. There is no suggestion to use an oridonin-containing extract.

GB 1476016 and JP 52-102434 to Fujita et al. ("Fujita") belong to the same patent family and disclose pharmaceutical compositions comprising oridonin and/or lasiokaurin as antitumor agents. The pharmaceutical compositions are prepared from isolated oridonin and/or lasiokaurin and further comprise a solid or liquid carrier. There is no contemplation of the therapeutic use of oridonin-containing plant extracts as antitumor agents.

According to the abstract provided with the 3/5/03 office action, JP 11-236334 discloses the use of twenty-three plants or their extracts as cell adhesion inhibitors or cancer metastasis inhibitors; the plants include, inter alia, *Humulus lupulus*.

According to the abstract provided with the 3/5/03 office action, JP 52-145509 alleges that “a bitter principle of hops of *Humulus lupulus*,” prepared by aqueous extraction of dried hops, exhibits an anti-cancer effect for cancers of the stomach, liver, lung, and breast.

Applicants respectfully assert that the Examiner does not appear to have given due consideration to the arguments in Applicants’ 6/4/02 amendment. For example, the Examiner states that “**All** of the references teach using their extract for treating cancer.” (8/26/03 office action, page 3, final paragraph; emphasis in original.) This argument ignores the fact that references cited as teaching oridonin, JP 57167938, GP1476016, and JP 352102434, describe the use of isolated compounds and therefore teach away from the use of oridonin-containing extracts. In contrast, the references cited as teaching lupulone, JP 11-236334 and JP 52-145509, do not mention any isolated compounds and instead teach the use of plants (JP 11-236334) or their extracts (JP 11-236334 and JP 52-145509). Thus, when the references are considered as a whole – as they must be – the different forms of the respective compositions teach away from the suggested combination of references. Furthermore, if the Examiner is relying on the teachings of JP 11-236334, there is no suggestion to select *Humulus lupulus* from among the 23 plants taught by the reference. And if the Examiner is relying on the teachings of JP 52-145509, there is no suggestion to add any extraneous substance, let alone isolated oridonin, to the aqueous extract of *Humulus lupulus*. Because there is no objective teaching to combine the references to obtain Applicants’ invention, a prima facie case has not been established.

The Examiner has also failed to address Applicants’ arguments with respect to expectation of success. The Examiner is referred to Applicants’ 6/4/03 amendment for the complete arguments, but to summarize, the cited references provide no expectation of success for the combination of oridonin (or salt, ester, or analog thereof) and lupulone (or

salt, ester, or analog thereof) recited in Applicants' Claim 1. And although the Examiner has cited case law for the proposition that it is obvious to combine two or more ingredients useful for the same purpose, these cases are inapposite because they do not deal with the notoriously unpredictable pharmaceutical arts. In summary, the cited references, taken together with the knowledge of one skilled in the art of cancer treatment and considered in light of the unpredictability of the pharmaceutical arts, provide no expectation of success for Applicants' Claim 1 composition.


For these reasons, Applicants maintain that a prima facie case of obviousness has not been established. Given that Claims 10, 17, 25, 31, 36, and 37 have been canceled, Applicants respectfully request the reconsideration and withdrawal of the rejection of Claims 1-9, 11-16, 18-23, 26-29, and 32-35 under 35 U.S.C. § 103(a).

It is believed that the foregoing amendments and remarks fully comply with the Office Action and that the claims herein should now be allowable to Applicants. Accordingly, reconsideration and allowance is requested.

If there are any additional charges with respect to this Amendment or otherwise, please charge them to Deposit Account No. 06-1130 maintained by Applicants' Attorneys.

Respectfully submitted,

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